

	L #	Hits	Search Text	Time Stamp
1	L1	6023	435/4,7.1.ccls.	2002/10/19 09:49
2	L2	13324	mass adj spectrometry	2002/10/19 09:50
3	L3	446	1 and 2	2002/10/19 09:50
4	L4	3885	435/7.1.ccls.	2002/10/19 09:50
5	L5	338	4 and 2	2002/10/19 09:51
6	L6	10151	internal adj standard	2002/10/19 09:52
7	L7	18	5 and 6	2002/10/19 10:00
8	L8	661	(mass adj spectrometry).clm,ab.	2002/10/19 10:01
9	L9	39	1 and 8	2002/10/19 10:01

L8 ANSWER 1 OF 43 MEDLINE

ACCESSION NUMBER: 2002180652 MEDLINE

DOCUMENT NUMBER: 21910177 PubMed ID: 11913536

TITLE: ***Mass*** ***spectrometric*** separation and
determination of N1,N12-diacetylspermine in the urine of
cancer patients.

AUTHOR: Kobayashi Masaki; Samejima Keijiro; Hiramatsu Kyoko;
Kawakita Masao

CORPORATE SOURCE: Department of Analytical Chemistry, Faculty of
Pharmaceutical Sciences, Josai University, Sakado, Saitama,
Japan.

SOURCE: BIOLOGICAL AND PHARMACEUTICAL BULLETIN, (2002 Mar) 25 (3)
372-4.

Journal code: 9311984. ISSN: 0918-6158.

PUB. COUNTRY: Japan

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200210

ENTRY DATE: Entered STN: 20020401

Last Updated on STN: 20021002

Entered Medline: 20021001

AB An ionspray ionization ***mass*** - ***spectrometric*** method for
the determination of N1,N12-diacetylspermine (Ac2Spm) was developed using
15N-labeled Ac2Spm as the ***internal*** ***standard***.
Concentrations of Ac2Spm in the urine obtained from 17 cancer patients
measured by the present method correlated well with those measured by
ELISA, showing the usefulness of the two methods.

L8 ANSWER 2 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:356520 BIOSIS

DOCUMENT NUMBER: PREV200200356520

TITLE: Sensitive and simultaneous determination of HIV protease
inhibitors in rat biological samples by liquid
chromatography- ***mass*** ***spectrometry***.

AUTHOR(S): Gao, Weihua; Kishida, Tomoyuki; Kimura, Keisuke; Kageyama,
Michiharu; Sumi, Masaki; Yoshikawa, Yukako; Shibata,
Nobuhito (1); Takada, Kanji

CORPORATE SOURCE: (1) Department of Pharmacokinetics, Kyoto Pharmaceutical
University, Nakauchi-cho 5, Misasagi Yamashina-ku, Kyoto,
607-8414: shibata@mb.kyoto-phu.ac.jp Japan

SOURCE: Biomedical Chromatography, (June, 2002) Vol. 16, No. 4, pp.
267-273. print.

ISSN: 0269-3879.

DOCUMENT TYPE: Article

LANGUAGE: English

AB A sensitive and simultaneous liquid chromatographic- ***mass***
spectrometric (LC/MS) method for the determination of current four
HIV protease inhibitors (PIs), indinavir (IDV), saquinavir (SQV),
nelfinavir (NFV) and amprenavir (APV) in rat plasma and liver dialysate by
a microdialysis method was described. An isocratic LC/MS method in
combination with atmospheric pressure chemical ionization was developed
for the determination of these four PIs in biological samples in the same
run. The analytes including an ***internal*** ***standard*** were
extracted from 100 µL of plasma or 150 µL of liver dialysate samples by
salting-out with 100 µL of ice-cold 2 M K3PO4 followed by ether
extraction. The separation of analytes was carried out on a reversed-phase
semi-micro column using 50% of acetonitrile containing 1% acetic acid as
mobile phase at a flow rate of 0.2mL/min-1. The separation was completed
within 5 min. Precision, recovery and limits of detection indicated that
the method was suitable for the quantitative determination of these PIs in
rat plasma or liver dialysate. This simple, sensitive and highly specific
LC/MS method is suitable for pharmacokinetic studies and therapeutic drug
monitoring in AIDS patients who receive double protease therapy.

L8 ANSWER 3 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:484132 BIOSIS

DOCUMENT NUMBER: PREV200200484132

TITLE: Analysis of betamethasone in rat plasma using automated solid-phase extraction coupled with liquid chromatography-tandem ***mass*** ***spectrometry***
 . Determination of plasma concentrations in rat following oral and intravenous administration.

AUTHOR(S): Tamvakopoulos, C. S. (1); Neugebauer, J. M.; Donnelly, M.; Griffin, P. R.

CORPORATE SOURCE: (1) Merck Research Laboratories, Rahway, NJ, 07065 USA

SOURCE: Journal of Chromatography B, (5 September, 2002) Vol. 776, No. 2, pp. 161-168. <http://www.elsevier.com/locate/jchromb>. print.
 ISSN: 1387-2273.

DOCUMENT TYPE: Article

LANGUAGE: English

AB A method is described for the determination of betamethasone in rat plasma by liquid chromatography-tandem ***mass*** ***spectrometry*** (LC-MS-MS). The analyte was recovered from plasma by solid-phase extraction and subsequently analyzed by LC-MS-MS. A Packard Multiprobe II, an automated liquid handling system, was employed for the preparation and extraction of a 96-well plate containing unknown plasma samples, standards and quality control samples in an automated fashion. Prednisolone, a structurally related steroid, was used as an ***internal***
 standard. Using the described approach, a limit of quantitation of 2 ng/ml was achieved with a 50 µl aliquot of rat plasma. The described level of sensitivity allowed the determination of betamethasone concentrations and subsequent measurement of kinetic parameters of betamethasone in rat. Combination of automated plasma extraction and the sensitivity and selectivity of LC-MS-MS offers a valuable alternative to the methodologies currently used for the quantitation of steroids in biological fluids.

L8 ANSWER 4 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:191809 BIOSIS

DOCUMENT NUMBER: PREV200200191809

TITLE: High-performance liquid chromatographic-tandem ***mass***
 spectrometric evaluation and determination of stable isotope labeled analogs of rofecoxib in human plasma samples from oral bioavailability studies.

AUTHOR(S): Chavez-Eng, C. M. (1); Constanzer, M. L.; Matuszewski, B. K.

CORPORATE SOURCE: (1) Merck Research Laboratories, West Point, PA, 19486 USA

SOURCE: Journal of Chromatography B, (5 February, 2002) Vol. 767, No. 1, pp. 117-129. print.
 ISSN: 0378-4347.

DOCUMENT TYPE: Article

LANGUAGE: English

AB A method for the simultaneous determination of a cyclooxygenase-2 inhibitor, 4-(4-methanesulfonylphenyl)-3-phenyl-5H-furan-2-one (rofecoxib, I) and (13C7)rofecoxib, (II), in human plasma has been developed to support the clinical oral bioavailability (BA) study of I. The method is based on high-performance liquid chromatography (HPLC) with atmospheric pressure chemical ionization tandem ***mass*** ***spectrometric*** (APCI-MS-MS) detection in the negative ionization mode using a heated nebulizer interface. Two different stable isotope labeled analogs of I were initially evaluated for their use as intravenous (i.v.) markers in the BA study. (13CD3)Rofecoxib was shown to be isotopically unstable in plasma and water containing solvent and an efficient deuterium exchange prevented its use in the study. On the other hand, the isotopic integrity of the subsequently synthesized (13C7)rofecoxib (II) was maintained, as expected, in plasma and other solvent systems. The results of these experiments clearly demonstrated the need for the careful evaluation of the isotopic integrity of the stable isotope labeled compound for the successful utilization of these compounds in BA studies and also as internal standards in the quantitative analysis of drugs in biological fluids. After liquid-liquid extraction of I, II, and ***internal***
 standard (III) from plasma, the analytes were chromatographed on a

narrow bore (100 mmX3.0 mm) C18 analytical column, with mobile phase consisting of acetonitrile-water (1:1, v/v) at a flow-rate of 0.5 ml/min. The MS-MS detection was performed on a PE Sciex API III Plus tandem ***mass*** ***spectrometer*** operated in the selected reaction monitoring mode. The precursor/product ion combinations of m/z 313/257, 320/292, and 327/271 were used to quantify I, II, and III, respectively. The assay was validated in the concentration range of 0.1 to 100 ng/ml of plasma for both I and II. The precision of the assay (expressed as relative standard deviation) was less than 10% at all concentrations within the standard curve range, with adequate assay accuracy. The assay was utilized to support the clinical BA study in which oral doses of I were administered together with an i.v. dose of II to determine the oral BA of rofecoxib at 12.5- and 25-mg doses.

L8 ANSWER 5 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:178587 BIOSIS

DOCUMENT NUMBER: PREV200200178587

TITLE: Rapid liquid chromatography-tandem ***mass*** ***spectrometry*** method for routine analysis of cyclosporin A over an extended concentration range.

AUTHOR(S): Keavii, Brian G. (1); Tierney, David P.; Cooper, Donald P.; Morris, Michael R.

CORPORATE SOURCE: (1) Department of Clinical Biochemistry, Wythenshawe Hospital, Manchester, M23 9LT: bkeevil@smuht.nwest.nhs.uk UK

SOURCE: Clinical Chemistry, (January, 2002) Vol. 48, No. 1, pp. 69-76. print.
ISSN: 0009-9147.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Background: Cyclosporin A (CsA) is commonly measured by ***immunoassay*** techniques that have a limited analytical range. The consequence of this is that low CsA concentrations that may be clinically significant are difficult to measure and that high concentrations require sample dilution, which introduces error and increases cost. More specific assays, such as HPLC, do not have the required turnaround times for busy transplant clinics. Methods: CsA was measured in whole blood from 180 cardiac and lung transplant recipients by a liquid chromatography-tandem ***mass*** ***spectrometry*** (MS) assay, and the results were compared with the Dade Behring Emit assay. Proteins were precipitated with acetonitrile containing ascomycin as ***internal*** ***standard***. We used isocratic elution on a Supelco CN column (33 X 3.0 mm; 3-µm bead size) with a mobile phase of 65% aqueous acetonitrile containing ammonium acetate (2 mmol/L) and formic acid (1 g/L), at a flow rate of 0.5 mL/min, with a sample injection volume of 6 µL. We used positive-ion electrospray MS to monitor the ammonium adducts of the compounds of interest decomposing under controlled conditions to the most dominant fragments of the individual molecules. Calibration curves used linear least-squares regression with 1/x weighting. Results: Maximum sensitivity was obtained by monitoring fragmentation of the ammonium adducts m/z 1220/1203 for CsA and m/z 809/765 for ascomycin. Sample throughput, including preparation time, was 30 samples in 1.5 h with an injection-to-injection cycle time of 1.5 min. The calibration curve was linear to 5000 µg/L, with a detection limit of 0.03 µg/L and a limit of quantification of 1 µg/L. Regression analysis (tandem MS method (y) and Emit assay (x)) yielded a slope of 1.09 (+/- 0.03), an intercept of 6.2 (+/- 4.5) µg/L, and Sy/x = 27 µg/L. Conclusions: Tandem MS assay is a realistic alternative to ***immunoassay*** for the routine monitoring of CsA in transplant recipients. Its wide dynamic range has utility for pharmacokinetic studies of CsA.

L8 ANSWER 6 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2002:291262 BIOSIS

DOCUMENT NUMBER: PREV200200291262

TITLE: Quantification of sirolimus by liquid chromatography-tandem ***mass*** ***spectrometry*** using on-line solid-phase extraction.

AUTHOR(S): Vogeser, Michael (1); Fleischer, Claudia; Meiser, Bruno;
Groetzner, Jan; Spoehrer, Ute; Seidel, Dietrich
CORPORATE SOURCE: (1) Institut fuer Klinische Chemie, Klinikum der
Universitaet Muenchen-Grosshadern, 81366, Munich:
mvogeser@klch.med.uni-muenchen.de Germany
SOURCE: Clinical Chemistry and Laboratory Medicine, (January, 2002)
Vol. 40, No. 1, pp. 40-45. print.
ISSN: 1434-6621.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Quantification of the new ***immunosuppressant*** sirolimus (syn. rapamycin; Rapamune(R)) in whole blood by chromatography is essential for its clinical use since no ***immunoassay*** is available although monitoring is mandatory. Here we report on a rapid and convenient liquid chromatography (LC)-tandem ***mass*** ***spectrometry*** method and describe our practical experience with its routine use. Whole blood samples were hemolyzed and deproteinized using an equal volume (150 µl) of a mixture of methanol/zinc sulfate solution containing the ***internal*** ***standard*** desmethoxy-rapamycin. After centrifugation, the clear supernatants were submitted to an on-line solid-phase extraction procedure using the polymeric Waters Oasis HLB(R) material, with elution of the extracts onto the analytical column in the back-flush mode by column switching. For analytical chromatography a RP-C18 column was used with 90/10 methanol/2 mM ammonium acetate as the mobile phase. A 1:10 split was used for the transfer to the ***mass*** ***spectrometer***, a Micromass Quattro LC-tandem ***mass*** ***spectrometry*** system equipped with a Z-spray(R) source and used in the positive electrospray ionization mode. The following transitions were recorded: sirolimus, 931>864 m/z, and desmethoxy-rapamycin (I.S.), 901>834 m/z. The analytical running time was 5 min, including on-line extraction. The method has a linear calibration curve ($r > 0.99$; range 1.6-50 µg/l) and is rugged and precise with monthly CVs <7% at a sirolimus concentration of 13.1 µg/l in routine use; the instrumentation proved to be reliable and required minimal maintenance.

L8 ANSWER 7 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:451071 BIOSIS

DOCUMENT NUMBER: PREV200100451071

TITLE: Growth hormone abuse in the horse: Preliminary assessment of a ***mass*** ***spectrometric*** procedure for IGF-I identification and quantitation.

AUTHOR(S): de Kock, Schalk S. (1); Rodgers, John P.; Swanepoel, Beatrix C.

CORPORATE SOURCE: (1) The Laboratory of the Jockey Club of Southern Africa, Turffontein, 2140: schalkdk@iafrica.com South Africa

SOURCE: Rapid Communications in Mass Spectrometry, (2001) Vol. 15, No. 14, pp. 1191-1197. print.
ISSN: 0951-4198.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Previous studies have shown that insulin-like growth factor I (IGF-I) is a promising marker for the detection of growth hormone (GH) abuse in the horse. The significant increases observed with GH administration in comparison to natural levels imply the possibility of setting a threshold level for IGF-I that would be indicative of GH abuse. Although an ***immunoradiometric*** assay (IRMA) has been identified as a reliable screening method, a more specific IGF-I quantification method needs to be developed for the prosecution of GH abuse by horseracing authorities. This study describes such an HPLC electrospray ***mass*** ***spectrometry*** (LC/ESI-MS) method that was developed and then assessed for the specific analysis of IGF-I at the low levels encountered in serum. The structural identity of IGF-I was confirmed by endoproteinase Asp-N digestion followed by LC/MS and LC/MS/MS characterisation. This was followed by quantification of IGF-I as the intact molecule against an ***internal*** ***standard***.

L8 ANSWER 8 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:373101 BIOSIS

DOCUMENT NUMBER: PREV200100373101

TITLE: High-throughput semi-automated 96-well liquid/liquid extraction and liquid chromatography/ ***mass***
spectrometric analysis of everolimus (RAD 001) and cyclosporin A (CsA) in whole blood.

AUTHOR(S): Brignol, Nasty; McMahon, Louis M. (1); Luo, Suyi; Tse, Francis L. S.

CORPORATE SOURCE: (1) Novartis Pharmaceuticals Corporation, 59 Route 10, Building 405, Room 231, East Hanover, NJ, 07936:
louis.mcmahon@pharma.novartis.com USA

SOURCE: Rapid Communications in Mass Spectrometry, (25 May, 2001)
Vol. 15, No. 12, pp. 898-907. print.
ISSN: 0951-4198.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A semi-automated high-throughput liquid/liquid extraction (LLE) assay was developed for RAD001 and cyclosporin A (CsA) in human blood. After addition of ***internal*** ***standard*** and ammonium hydroxide, samples were extracted twice with methyl tert-butyl ether (MTBE). The organic extract was evaporated to dryness and reconstituted in mobile phase. Where possible, sample transfer and LLE steps were automated using a Tomtec Quadra 96 workstation. Samples were analyzed using ESI-LC/MS/MS employing the transitions of ((M+NH₄)+fwdarw(M+H)+) for CsA and ((M+NH₄)+fwdarw(M+H-(CH₃OH+H₂O))+) for RAD001, under isocratic chromatographic conditions (75:25, (v/v), acetonitrile/20 mM ammonium acetate) with a run time of 3.6 min. A lower limit of quantitation (LLOQ) of 0.368 ng/mL and 5.23 ng/mL was achieved for RAD001 and CsA, respectively, using a sample volume of 0.3 mL for the analysis. The method was validated over a 3-day period and the resulting calibration curves had a correlation coefficient >0.99 over the concentration range 0.368 to 409 ng/mL and 5.24 to 1748 ng/mL for RAD001 and CsA, respectively. The inter-day coefficient of variation (CV) was less than 15% at the LLOQ for both compounds. The method was applied to the analysis of clinical samples. Under normal working conditions four 96-well plates could be extracted and LC/MS analysis completed in less than 28 h. A marked improvement in sample throughput efficiency was realized with this LLE method when compared to existing solid phase extraction (SPE) methods which deal with both RAD001 and CsA.

L8 ANSWER 9 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 2002006504 EMBASE

TITLE: High performance liquid chromatography - Ion trap
mass ***spectrometry*** for the determination
of Insulin-like Growth Factor-I in horse plasma.

AUTHOR: Popot M.A.; Bobin S.; Bonnaire Y.; Pirens G.; Closset J.;
Delahaut Ph.; Tabet J.C.

CORPORATE SOURCE: M.A. Popot, LAB/FNCF, 169 Avenue de la Division Leclerc,
92290 Chateaufort-Malabry, France

SOURCE: Chromatographia, (2001) 54/11-12 (737-741).

Refs: 10

ISSN: 0009-5893 CODEN: CHRGB7

COUNTRY: Germany

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 027 Biophysics, Bioengineering and Medical
Instrumentation

029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Insulin-like Growth Factor I is a marker of Somatotropin administration.

In order to quantify this peptide in horse plasma samples, a high performance liquid chromatography/electrospray ***mass***
spectrometry method using R3 Insulin-like Growth Factor I as
internal ***standard*** was developed. The extraction
procedure involves an acid ethanol extraction and an

immunoaffinity ***purification***. Quantification is made possible by using deconvolution software and by measuring the Insulin like growth factor-I/ ***internal*** ***standard*** ratio. Comparison between high performance liquid chromatography/electrospray ***mass*** ***spectrometry*** and two ***immunological*** methods indicated agreement between methods even though more samples are needed to confirm this finding.

L8 ANSWER 10 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:390495 BIOSIS

DOCUMENT NUMBER: PREV200100390495

TITLE: Quantitation of cyclosporin A in whole blood by liquid chromatography/stable isotope dilution electrospray ionization ***mass*** ***spectrometry***.

AUTHOR(S): Magni, F. (1); Pereira, S.; Leoni, M.; Grisenti, G.; Kienle, M. Galli

CORPORATE SOURCE: (1) Laboratorio di Spettrometria di Massa, IRCCS San Raffaele, Via Olgettina 50, 20132, Milan: magni.fulvio@hsr.it Italy

SOURCE: Journal of Mass Spectrometry, (June, 2001) Vol. 36, No. 6, pp. 670-676. print. ISSN: 1076-5174.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Therapy with cyclosporin A (CsA) for ***immunosuppression*** after organ transplantation requires monitoring of its levels in blood owing of the narrow therapeutic index of the drug and to the high inter-individual variability of the drug absorption and metabolism. We describe the preparation of CsA labelled with stable isotopes (¹³C and ²H) with an isotopic enrichment of about 99% using labelled glucose and its use as ***internal*** ***standard*** for quantification of CsA blood levels by isotope dilution/electrospray ionization ***mass*** ***spectrometry***. The method was found to be linear in the tested range (1-1000 ng) with and without the matrix. The accuracy of the bracketing calibration curves prepared using 100 ng ml⁻¹ labelled CsA was within +1.7% (bias). The results confirmed the usefulness of the procedure as a reference method for the external quality assessment of the field methods for the evaluation of CsA blood concentration, the imprecision (relative standard deviation) and accuracy (bias) being <2%.

L8 ANSWER 11 OF 43 MEDLINE

ACCESSION NUMBER: 2001386812 MEDLINE

DOCUMENT NUMBER: 21334185 PubMed ID: 11440728

TITLE: Simultaneous simple and fast quantification of three major ***immunosuppressants*** by liquid chromatography--tandem ***mass*** - ***spectrometry***.

AUTHOR: Volosov A; Napoli K L; Soldin S J

CORPORATE SOURCE: Department of Laboratory Medicine, Children's National Medical Center, 111 Michigan Ave. NW, Washington, DC 20010-2970, USA.

SOURCE: CLINICAL BIOCHEMISTRY, (2001 Jun) 34 (4) 285-90. Journal code: 0133660. ISSN: 0009-9120.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200109

ENTRY DATE: Entered STN: 20011001

Last Updated on STN: 20011001

Entered Medline: 20010927

AB OBJECTIVES: The aim of the current study was to develop a simple, fast and universal method for quantification of any combination of the three major ***immunosuppressants*** sirolimus, tacrolimus and cyclosporin in whole blood, using a LC-tandem ***mass*** ***spectrometer*** (API-2000, SCIEX, Toronto, Canada). METHODS: 250 microL whole blood was spiked with ***internal*** ***standard*** (ritonavir), and protein precipitated

with 350 microL acetonitrile. The sample was centrifuged and 30 microL aliquot was injected onto the HPLC column, where it underwent an online extraction with ammonium acetate. After that the automatic switching valve was activated, changing the mobile phase to methanol and thereby eluting the analytes into the tandem ***mass*** ***spectrometer***. The high selectivity of a tandem mass analyzer allows determination of any combination of the three drugs within a 5 min run. RESULTS: Between-day precision was between 2.4% and 9.7% for all analytes at the concentrations tested. Accuracy ranged between 98.8% and 103.2% (n = 20). The method was linear over the measuring ranges of all analytes. Within-run precision was below %CV = 6% for all analytes. Good correlation with other analytical methods was observed. CONCLUSIONS: The simplicity, universality and high throughput of the method make it suitable for application in a clinical laboratory. The method has been implemented in our laboratory for a routine use.

L8 ANSWER 12 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:497004 BIOSIS

DOCUMENT NUMBER: PREV200100497004

TITLE: Determination of celecoxib in human plasma and rat microdialysis samples by liquid chromatography tandem ***mass*** ***spectrometry***.

AUTHOR(S): Braeutigam, Lutz; Vetter, Gregor; Tegeder, Irmgard; Heinkle, Georg; Geisslinger, Gerd (1)

CORPORATE SOURCE: (1) Pharmazentrum Frankfurt, Klinikum der Johann Wolfgang Goethe-Universitaet Frankfurt, Theodor Stern Kai 7, D-60590, Frankfurt am Main: geisslinger@em.uni-frankfurt.de Germany

SOURCE: Journal of Chromatography B, (25 September, 2001) Vol. 761, No. 2, pp. 203-212. print. ISSN: 0378-4347.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Methods for the determination of celecoxib in human plasma and rat microdialysis samples using liquid chromatography tandem ***mass*** ***spectrometry*** are described. Celecoxib and an ***internal*** ***standard*** were extracted from plasma by solid-phase extraction with C18 cartridges. Thereafter compounds were separated on a short narrow bore RP C18 column (30X2 mm). Microdialysis samples did not require extraction and were injected directly using a narrow bore RP C18 column (70X2 mm). The detection was by a PE Sciex API 3000 ***mass*** ***spectrometer*** equipped with a turbo ion spray interface. The compounds were detected in the negative ion mode using the mass transitions m/z 380fwdarw316 and m/z 366fwdarw302 for celecoxib and ***internal*** ***standard***, respectively. The assay was validated for human plasma over a concentration range of 0.25-250 ng/ml using 0.2 ml of sample. The assay for microdialysis samples (50 mul) was validated over a concentration range of 0.5-20 ng/ml. The method was utilised to determine pharmacokinetics of celecoxib in human plasma and in rat spinal cord perfusate.

L8 ANSWER 13 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:262707 BIOSIS

DOCUMENT NUMBER: PREV200100262707

TITLE: Liquid chromatographic-tandem ***mass*** ***spectrometric*** determination of amprenavir (agenerase) in serum/plasma of human ***immunodeficiency*** virus type-1 infected patients receiving combination antiretroviral therapy.

AUTHOR(S): Gunawan, Sonny (1); Griswold, Marshall P.; Kahn, Douglas G.

CORPORATE SOURCE: (1) Consolidated Laboratory Services, 7855 Haskell Avenue, Suite 302, Van Nuys, CA, 91406-1902: sgunawan@pacificoaks.com USA

SOURCE: Journal of Chromatography A, (20 April, 2001) Vol. 914, No. 1-2, pp. 1-4. print. ISSN: 0021-9673.

DOCUMENT TYPE: Article
 LANGUAGE: English
 SUMMARY LANGUAGE: English

AB A selective assay method for quantitation of amprenavir (agenerase) in human ***immunodeficiency*** virus type-1 infected patient serum or plasma using liquid chromatography-tandem ***mass*** spectrometry*** (LC-MS-MS) is described. Amprenavir and an ***internal*** standard*** (reserpine) are extracted by liquid-liquid extraction and chromatographically separated by a reversed-phase C18-analytical column. The triple quadrupole LC-MS-MS system is operated in the positive-ion mode and multiple reaction monitoring is used for drug quantitation. The method has been validated over the range of 0.05-10.0 mug/ml. The RSDs for the intra-day and inter-day determinations ranged from 5.3 to 6.1% and from 4.7 to 6.2%, respectively. The average assay accuracy at two different concentrations ranged from 96.0 to 103.0% and the extraction recovery of amprenavir was 90.8%. The lower limit of quantitation was 0.05 mug/ml. Using a short microbore column, the analysis was completed in less than 5 min.

L8 ANSWER 14 OF 43 MEDLINE DUPLICATE 1

ACCESSION NUMBER: 2000499025 MEDLINE

DOCUMENT NUMBER: 20393400 PubMed ID: 10939406

TITLE: Detection and quantification of neurotensin in human brain tissue by matrix-assisted laser desorption/ionization
 time -of- ***flight*** ***mass*** spectrometry***

AUTHOR: Gobom J; Kraeuter K O; Persson R; Steen H; Roepstorff P; Ekman R

CORPORATE SOURCE: Neurochemistry Section, Institute of Clinical Neuroscience, SU/Moelndal Hospital, Goteborg University, Sweden.

SOURCE: ANALYTICAL CHEMISTRY, (2000 Jul 15) 72 (14) 3320-6.
 Journal code: 0370536. ISSN: 0003-2700.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200010

ENTRY DATE: Entered STN: 20001027

Last Updated on STN: 20001027

Entered Medline: 20001017

AB A method was developed for ***mass*** spectrometric*** detection of neurotensin (NT)-like ***immunoreactivity*** and quantification of NT in human brain tissue. The method is based on ***immunoprecipitation*** followed by analysis using matrix-assisted laser desorption/ionization ***time*** -of- ***flight*** ***mass*** spectrometry*** (***MALDI*** -TOF-MS). The identity of the major component of the ***immunoprecipitates*** as neurotensin was confirmed by fragment ion analysis on an electrospray ionization quadrupole ***time*** -of- ***flight*** instrument. ***MALDI*** -TOF-MS quantification of NT was achieved using stable-isotope-labeled NT as the ***internal*** standard***, yielding an error of less than 5%. The method allowed detection of low-femtomole amounts of NT, starting from low-milligram amounts of lyophilized brain tissue. In addition to NT, several other peptides were detected in the ***purified*** samples, most of which, according to their molecular masses, corresponded to fragments of NT. The method is demonstrated with quantification of NT from human hypothalamus tissue, and a comparison is made with results obtained from competitive radioimmunoassay.

L8 ANSWER 15 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2001:43633 BIOSIS

DOCUMENT NUMBER: PREV200100043633

TITLE: High-throughput analysis of everolimus (RAD001) and cyclosporin A (CsA) in whole blood by liquid chromatography/ ***mass*** spectrometry*** using a semi-automated 96-well solid-phase extraction system.

AUTHOR(S): McMahon, Louis M. (I); Luo, Suyi; Hayes, Michael; Tse,

Francis L. S.

CORPORATE SOURCE: (1) Novartis Pharmaceuticals Corporation, 59 Route 10,
Building 405, Room 231, East Hanover, NJ, 07936:
louis.mcmahon@pharma.novartis.com USA

SOURCE: Rapid Communications in Mass Spectrometry, (2000) Vol. 14,
No. 21, pp. 1965-1971. print.
ISSN: 0951-4198.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A semi-automated solid-phase extraction (SPE) liquid chromatography/
mass ***spectrometry*** (LC/MS) procedure was validated for
the simultaneous determination of everolimus (RAD001) and cyclosporin A
(CsA) in human blood. Whole blood samples (350 µL) were pretreated with
acetonitrile/zinc sulfate mixture to precipitate the sample proteins. The
samples were centrifuged and the resulting supernatants were manually
transferred to a 96-well plate format. All subsequent sample transfer and
solid phase extraction was automated using a Tomtec Quadra 96 workstation.
Samples were analyzed by LC/MS using an atmospheric pressure chemical
ionization (APCI) interface. In order to enhance sensitivity, the MS
method used negative ion mode for RAD001 ((M)-) and its ***internal***
standard and positive ion mode for CsA ((M + H)+) and its
internal ***standard***. The lower limit of quantitation was
0.375 ng.mL⁻¹ for RAD001 and 6.95 ng.mL⁻¹ for CsA. The reproducibility of
the method was evaluated by analyzing six replicates at five or more
quality control (QC) levels over the nominal concentration range 0.375 to
253 ng.mL⁻¹ for RAD001 and 6.95 to 1530 ng.mL⁻¹ for CsA. The inter- and
intra-day accuracy was found to range from 89.7 to 114% with precision (%
CV) of less than 12% for both compounds. The sensitivity, small sample
volume needed and high sample throughput of this method make it an
attractive option for pharmacokinetic studies in pediatric patients.

L8 ANSWER 16 OF 43 MEDLINE DUPLICATE 2

ACCESSION NUMBER: 2000473151 MEDLINE

DOCUMENT NUMBER: 20341804 PubMed ID: 10884300

TITLE: Measurement of apolipoprotein B concentration in plasma
lipoproteins by combining selective precipitation and
mass ***spectrometry***.

AUTHOR: Beghin L; Duhal N; Poulain P; Hauw P; Lacroix B; Lecerf J
M; Bonte J P; Fruchart J C; Luc G

CORPORATE SOURCE: Department of Atherosclerosis, Institut Pasteur de Lille,
France.

SOURCE: JOURNAL OF LIPID RESEARCH, (2000 Jul) 41 (7) 1172-6.
Journal code: 0376606. ISSN: 0022-2275.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200010

ENTRY DATE: Entered STN: 20001012

Last Updated on STN: 20001012

Entered Medline: 20001005

AB The measurement of apolipoprotein B (apoB) in ***purified***
lipoproteins by ***immunological*** assays is subject to criticism
because of denatured epitopes or ***immunoreactivity*** differences
between ***purified*** lipoproteins and standard. Chemical methods
have therefore been developed, such as the selective precipitation of apoB
followed by quantification of the precipitate. In this study, we present
the measurement of apoB concentration in lipoproteins ***purified***
by ultracentrifugation by combining isopropanol precipitation and gas
chromatography/ ***mass*** ***spectrometry***. Very low density
lipoprotein (VLDL; $d < 1.006$ g/mL); VLDL plus intermediate density
lipoprotein (VLDL + IDL; $d < 1.019$ g/mL); and VLDL, IDL, and low density
lipoprotein (VLDL + IDL + LDL; $d < 1.063$ g/mL) were ***purified*** by
ultracentrifugation. Apolipoprotein B-100 was selectively precipitated by
isopropanol. The leucine content of the pellet was then determined by gas
chromatography/ ***mass*** ***spectrometry***, using norleucine as

internal ***standard*** . Knowledge of the number of leucine molecules in one apoB-100 molecule makes it possible to calculate the plasma concentration of apoB in the various lipoprotein fractions. ApoB in IDL (d 1.006-1.019 g/mL) and LDL (d 1.019-1.063 g/mL) were then determined by subtracting VLDL-apoB from apoB in lipoproteins d < 1.019 and apoB in lipoproteins d < 1.019 g/mL from apoB in lipoproteins d < 1.063 g/mL, respectively. The isopropanol precipitate was verified as pure apoB (>97%) in lipoprotein fractions isolated from normo- and hyperlipidemic plasma and the method appeared reproducible. The combination of isopropanol precipitation and the GC/MS method appears therefore to be a precise and reliable method for kinetic and epidemiological studies.

L8 ANSWER 17 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:320080 BIOSIS

DOCUMENT NUMBER: PREV200000320080

TITLE: Determination of 21-hydroxydeflazacort in human plasma by high-performance liquid chromatography/atmospheric pressure chemical ionization tandem ***mass***
spectrometry . Application to bioequivalence study.

AUTHOR(S): Ifa, Demian R. (1); Moraes, Maria E.; Moraes, Manuel O.; Santagada, Vincenzo; Caliendo, Giuseppe; de Nucci, Gilberto

CORPORATE SOURCE: (1) Jesuino Marcondes Machado 415, Campinas, SP Brazil

SOURCE: Journal of Mass Spectrometry, (March, 2000) Vol. 35, No. 3, pp. 440-445. print.
ISSN: 1076-5174.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB A liquid chromatographic atmospheric pressure chemical ionization tandem ***mass*** ***spectrometric*** method is described for the determination of 21-hydroxydeflazacort in human plasma using dexamethasone 21-acetate as an ***internal*** ***standard*** . The procedure requires a single diethyl ether extraction. After evaporation of the solvent under a nitrogen flow, the analytes are reconstituted in the mobile phase, chromatographed on a C18 reversed-phase column and analyzed by ***mass*** ***spectrometry*** via a heated nebulizer interface where they are detected by multiple reaction monitoring. The method has a chromatographic run time of less than 5 min and a linear calibration curve with a range of 1-400 ng mL⁻¹ (r>0.999). The between-run precision, based on the relative standard deviation for replicate quality controls, was 5.5% (10 ng mL⁻¹), 1.0% (50 ng mL⁻¹) and 2.7% (200 ng mL⁻¹). The between-run accuracy was +7.1, 3.8 and 4.8% for the above concentrations, respectively. This method was employed in a bioequivalence study of two DFZ tablet formulations (Denacen from Marjan Industria e Comercio, Brazil, as a test formulation, and Calcort from Merrell Lepetit, Brazil, as a reference formulation) in 24 healthy volunteers of both sexes who received a single 30 mg dose of each formulation. The study was conducted using an open, randomized, two-period crossover design with a 7-day washout interval. The 90% confidence interval (CI) of the individual geometric mean ratio for Denacen/Calcort was 89.8-109.5% for area under the curve AUC(0-24 h) and 80.7-98.5% for C_{max}. Since both the 90% CI for AUC(0-24 h) and C_{max} were included in the 80-125% interval proposed by the US Food and Drug Administration, Denacen was considered bioequivalent to Calcort according to both the rate and extent of absorption.

L8 ANSWER 18 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:528350 BIOSIS

DOCUMENT NUMBER: PREV200000528350

TITLE: Quantification of free mycophenolic acid by high-performance liquid chromatography-atmospheric pressure chemical ionisation tandem ***mass***
spectrometry .

AUTHOR(S): Willis, Charlene; Taylor, Paul J. (1); Salm, Paul; Tett, Susan E.; Pillans, Peter I.

CORPORATE SOURCE: (1) Department of Medicine, Princess Alexandra Hospital, Ipswich Road, Woolloongabba, First Floor Lions Clinical Research Building, Brisbane, Queensland, 4102 Australia

SOURCE: Journal of Chromatography B, (1 October, 2000) Vol. 748,
No. 1, pp. 151-156. print.
ISSN: 0378-4347.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB To facilitate the investigation of free mycophenolic acid concentrations we developed a high-performance liquid chromatography tandem ***mass*** ***spectrometry*** method using indomethacin as an ***internal*** ***standard***. Free drug was isolated from plasma samples (500 µl) using ultrafiltration. The analytes were extracted from the ultrafiltrate (200 µl) using C18 solid-phase extraction. Detection was by selected reactant monitoring of mycophenolic acid (m/z 318.9fwdarw190.9) and the ***internal*** ***standard*** (m/z 356.0fwdarw297.1) with an atmospheric pressure chemical ionisation interface. The total chromatographic analysis time was 12 min. The method was found to be linear over the range investigated, 2.5-200 µg/l ($r>0.990$, $n=6$). The relative recovery of the method for the control samples studied (7.5, 40.0 and 150 µg/l) ranged from 95 to 104%. The imprecision of the method, expressed in terms of intra- and inter-day coefficients of variation, was <8 and <9%, respectively. Further, analysis of pooled patient plasma produced an intra-day imprecision of 6.6%. The signal-to-noise ratio at the limit of quantification (2.5 µg/l) was approximately 5:1. The mean absolute recovery ($n=6$) of mycophenolic acid and the ***internal*** ***standard*** were 76.0+/-13.5% and 86.0+/-9.1%, respectively. The method reported provides an accurate and precise quantification of free mycophenolic acid over a wide analytical range and thus can be used for routine monitoring and pharmacokinetic studies.

L8 ANSWER 19 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:528348 BIOSIS

DOCUMENT NUMBER: PREV200000528348

TITLE: Validated electrospray liquid chromatographic- ***mass*** ***spectrometric*** assay for the determination of the mushroom toxins alpha- and beta-amanitin in urine after ***immunoaffinity*** extraction.

AUTHOR(S): Maurer, Hans H. (1); Schmitt, Christian J.; Weber, Armin A.; Kraemer, Thomas

CORPORATE SOURCE: (1) Department of Toxicology, Institute of Pharmacology and Toxicology, University of Saarland, D-66421, Homburg (Saar) Germany

SOURCE: Journal of Chromatography B, (1 October, 2000) Vol. 748,
No. 1, pp. 125-135. print.
ISSN: 0378-4347.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Specific detection of amanitins in body fluids is necessary for an early diagnosis of an intoxication with amanita mushrooms. In this paper, a liquid chromatographic- ***mass*** ***spectrometric*** assay after ***immunoaffinity*** extraction (IAE-LC-MS) is described for the determination of alpha- and beta-amanitin in urine. The method has been validated according to the criteria established by the Journal of Chromatography B. The assay was found to be selective. The calibration curves for alpha- and beta-amanitin were linear from 5 to 75 ng/ml. Intra- and inter-day accuracy and precision were inside the required limits. Amatoxins in frozen urine samples or ***immunoaffinity*** extracts were stable for more than 6 months, and the IAE columns could be used more than fifty times without remarkable loss in performance. LOD for alpha- and beta-amanitin was 2.5 ng/ml and LOQ for both was 5.0 ng/ml. The absolute recoveries of alpha- and beta-amanitin were 63% and 58% for the low quality control and 61% and 57% for the high quality control. The absolute recovery for the ***internal*** ***standard*** gamma-amanitin methyl ether at 25 ng/ml was 60%. The analysis of 5 authentic urine samples from patients intoxicated by amanita mushrooms showed a good correlation between the results measured by radioimmunoassay and the IAE-LC-MS assay. A partial validation showed that the assay was

also suitable for plasma analysis.

L8 ANSWER 20 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 2000:30130 BIOSIS

DOCUMENT NUMBER: PREV200000030130

TITLE: Microdetermination of prostaglandin E2 in joint fluid in
rheumatoid arthritis patients using gas
chromatography/selected ion monitoring.

AUTHOR(S): Hishinuma, Takanori; Nakamura, Hironori; Sawai, Takashi;
Uzuki, Miwa; Itabash, Yoshio; Mizugaki, Michinao (1)

CORPORATE SOURCE: (1) Department of Pharmaceutical Sciences, Tohoku
University Hospital, 1-1, Seiry-machi, Aoba-ku, Sendai,
980-8574 Japan

SOURCE: Prostaglandins & Other Lipid Mediators, (Oct., 1999) Vol.
58, No. 2-4, pp. 179-186.
ISSN: 1098-8823.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB We devised an effective ***purification*** for the microdetermination of prostaglandin E2 (PGE2) in human joint fluid using gas chromatography/selected ion monitoring and determined PGE2 in the joint fluid in rheumatoid arthritis (RA) patients using this method. The methyl ester-methoxime-tert-butyltrimethylsilyl ether derivative was prepared, then gas chromatography/selected ion monitoring was carried out by monitoring the ion at m/z 566.4 for PGE2 and at m/z 570.4 for the ***internal*** ***standard*** (PGE2-d4). A good linear response over the range of 10 pg to 50 ng was demonstrated. We detected PGE2 to a level of about 46 pg/ml in the joint fluid of RA patients. The level of PGE2 in RA patients was significantly higher than that in osteoarthritis patients used as controls. Moreover, we measured inflammatory cytokine (IL-1beta, TNFalpha, IL-6 receptor) levels in joint fluid by using enzyme-linked ***immunosorbent*** assay. A relationships between the PGE2 level in joint fluid and these cytokines or biochemical data as the indicator of RA disease was not observed. We found that the PGE2 level in each patient was influenced by therapeutic drugs. The PGE2 level in RA patients with non-steroidal anti-inflammatory drugs was lower than with steroids.

L8 ANSWER 21 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1999:496599 BIOSIS

DOCUMENT NUMBER: PREV199900496599

TITLE: Determination of zearalenone in grains by high-performance
liquid chromatography-tandem ***mass***
spectrometry after solid-phase extraction with
RP-18 columns or ***immunoaffinity*** columns.

AUTHOR(S): Zoellner, Peter; Jodlbauer, Justus; Lindner, W. (1)

CORPORATE SOURCE: (1) Institute of Analytical Chemistry, University of
Vienna, Waehringer Strasse 38, A-1090, Vienna Austria

SOURCE: Journal of Chromatography A, (Oct. 15, 1999) Vol. 858, No.
2, pp. 167-174.
ISSN: 0021-9673.

DOCUMENT TYPE: Article

LANGUAGE: English

SUMMARY LANGUAGE: English

AB In this paper a robust, sensitive and selective LC-MS-MS method for the determination of zearalenone (ZON) in several cereals is described. Sample preparation was performed by extraction of the commodities with a mixture of acetonitrile and water followed by solid-phase extraction with RP-18 columns or ***immunoaffinity*** columns. The selective determination of ZON was achieved with an atmospheric pressure chemical ionization interface. Using the negative ion mode a detection limit of 0.5 mug/kg and a determination limit of 1 mug/kg grain was achieved, which is by a factor of 100 more sensitive than the positive ion mode. Zearalanone (ZAN), which does not occur in nature, was used as ***internal*** ***standard*** for quantification. A linear working range from 1.0 mug/kg to 1000 mug/kg could be achieved in grains with a standard deviation of 4% and recovery rates around 100%. All these results were independent from the grain

matrices (maize, barley, oats, wheat) when ZAN was used as
 internal ***standard***. Sample preparation with RP-18 and
 immunoaffinity materials gave comparable results. In addition, the
 method was successfully used for the investigation of naturally
 contaminated maize samples in the course of an interlaboratory comparison
 test.

L8 ANSWER 22 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1999:45461 BIOSIS

DOCUMENT NUMBER: PREV199900045461

TITLE: Effect of the sample matrix on the determination of
 indinavir in human urine by HPLC with turbo ion spray
 tandem ***mass*** ***spectrometric*** detection.

AUTHOR(S): Fu, L.; Woolf, E. J. (1); Matuszewski, B. K.

CORPORATE SOURCE: (1) Dep. Drug Metabolism, Merck Res. Laboratories, West
 Point, PA 19486 USA

SOURCE: Journal of Pharmaceutical and Biomedical Analysis, (Nov.,
 1998) Vol. 18, No. 3, pp. 347-357.

ISSN: 0731-7085.

DOCUMENT TYPE: Article

LANGUAGE: English

AB The HPLC/tandem ***mass*** ***spectrometric*** (LC/MS/MS) behavior
 of indinavir, an HIV protease inhibitor, in human urine is presented as an
 example of a case where endogenous matrix components were found to
 interfere with the ionization of the target analyte. The MS/MS system used
 for these experiments was equipped with a turbo ion spray LC interface.
 Results from two sample preparation procedures (direct dilution of urine
 vs urine extraction) and two chromatographic systems (low vs. high
 capacity factor (k')) for the analytes were compared. Additionally, the
 precision of the analysis that was achieved while using a stable isotope
 labeled ***internal*** ***standard*** is contrasted with the
 results obtained using an analog of indinavir as ***internal***
 standard. The results obtained indicated that during development
 and validation of LC/MS/MS based assays the potential effect of co-eluting
 'unseen' endogenous species should be evaluated to ensure that sample
 preparation and chromatography is adequate to overcome the matrix effect
 problems.

L8 ANSWER 23 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1999:6025 BIOSIS

DOCUMENT NUMBER: PREV19990006025

TITLE: Quantitative analysis of sirolimus (Rapamycin) in blood by
 high-performance liquid chromatography-electrospray tandem
 mass ***spectrometry***.

AUTHOR(S): Taylor, Paul J. (1); Johnson, Anthony G.

CORPORATE SOURCE: (1) Cent. Clin. Exp. Therapeutics, Univ. Queensl., Dep.
 Med., Princess Alexandra Hosp., First Floor Lions Clin.
 Res. Build., Ipswich Rd., Brisbane, QLD 4102 Australia

SOURCE: Journal of Chromatography B, (Nov. 6, 1998) Vol. 718, No.
 2, pp. 251-257.

ISSN: 0378-4347.

DOCUMENT TYPE: Article

LANGUAGE: English

AB We report here a quantitative method for the analysis of sirolimus in
 blood using solid-phase sample preparation and HPLC-electrospray-tandem
 mass ***spectrometry*** detection. Blood samples (500 µl)
 were prepared by pre-treatment with acetonitrile: 15 mM zinc sulphate
 (70:30, v/v), containing 32-demethoxysirolimus (***internal***
 standard) and C18, solid-phase extraction. The electrospray
 conditions were chosen to enhance the (M+NH₄)⁺ species at the expense of
 other species. Detection was by multiple reactant monitoring with the mass
 transitions m/z 931.8fwdarw864.6 and m/z 901.8fwdarw834.4 employed for
 sirolimus and the ***internal*** ***standard***, respectively. The
 method was linear over the range 0.2 to 100.0 µg l⁻¹. The accuracy and
 inter-day precision, over this concentration range, was 94.4% to 104.4%
 and 1.4% to 5.0%, respectively. The accuracy and total precision at the
 limit of quantitation (0.2 µg l⁻¹) was 103.0% and 10.8%, respectively.

The mean absolute recovery of sirolimus and the ***internal***
 standard were 80.5% and 81.3%, respectively. The sensitivity and
 analytical concentration range of the method make it suitable for
 therapeutic drug monitoring and pharmacokinetic studies. Further, the
 ability of the method to measure parent drug specifically will facilitate
 the evaluation of ***immunoassays*** for sirolimus.

L8 ANSWER 24 OF 43 MEDLINE DUPLICATE 3
 ACCESSION NUMBER: 97201874 MEDLINE
 DOCUMENT NUMBER: 97201874 PubMed ID: 9049429
 TITLE: Analysis of the malondialdehyde-2'-deoxyguanosine adduct
 pyrimidopurinone in human leukocyte DNA by gas
 chromatography/electron capture/negative chemical
 ionization/ ***mass*** ***spectrometry***
 AUTHOR: Rouzer C A; Chaudhary A K; Nokubo M; Ferguson D M; Reddy G
 R; Blair I A; Marnett L J
 CORPORATE SOURCE: A.B. Hancock Jr. Memorial Laboratory for Cancer Research,
 Vanderbilt University School of Medicine, Nashville,
 Tennessee 37232, USA.
 CONTRACT NUMBER: CA47479 (NCI)
 CA68485 (NCI)
 ES00267 (NIEHS)
 +
 SOURCE: CHEMICAL RESEARCH IN TOXICOLOGY, (1997 Feb) 10 (2) 181-8.
 Journal code: 8807448. ISSN: 0893-228X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199705
 ENTRY DATE: Entered STN: 19970602
 Last Updated on STN: 19970602
 Entered Medline: 19970521

AB A method is described for the assay of the major malondialdehyde-
 deoxyguanosine adduct (M1G) based on ***immunoaffinity***
 purification and gas chromatography/electron capture/negative
 chemical ionization/ ***mass*** ***spectrometry***. A stable
 isotope of M1G-deoxyribose ([2H2]M1G-dR) was used as an ***internal***
 standard. Recovery of ***internal*** ***standard***
 throughout the entire assay procedure was approximately 40%. The assay
 showed a linear response over a range of 10-1000 pg of M1G-dR and was
 verified by analysis of a synthetic. M1G-containing oligomer. The limit of
 detection in biological samples was 100 fmol/sample, corresponding to 3
 adducts/10(8) bases for 1 mg of DNA. DNA was isolated from the blood of 10
 healthy human donors, and M1G levels were measured. A mean value of 6.2
 +/- 1.2 adducts/10(8) bases was obtained, with no obvious differences
 bases on age or cigarette smoking. A small, but statistically significant
 difference was observed between the levels in females (5.1 +/- 0.4
 adducts/10(8) bases) and males 6.7 +/- 1.1 adducts/10(8) bases). The
 presence of M1G in leukocyte DNA was further verified by analysis using
 liquid chromatography/electrospray ionization ***mass***
 spectrometry.

L8 ANSWER 25 OF 43 MEDLINE DUPLICATE 4
 ACCESSION NUMBER: 97126156 MEDLINE
 DOCUMENT NUMBER: 97126156 PubMed ID: 8971080
 TITLE: A stable isotope dilution assay for the in vivo
 determination of insulin levels in humans by ***mass***
 spectrometry
 AUTHOR: Stocklin R; Vu L; Vadas L; Cerini F; Kippen A D; Offord R
 E; Rose K
 CORPORATE SOURCE: Department of Medical Biochemistry, University of Geneva
 Medical Center, Switzerland.. reto.stocklin@medicine.unige.
 ch
 SOURCE: DIABETES, (1997 Jan) 46 (1) 44-50.
 Journal code: 0372763. ISSN: 0012-1797.
 PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
 ENTRY MONTH: 199701
 ENTRY DATE: Entered STN: 19970219
 Last Updated on STN: 19970219
 Entered Medline: 19970124

AB Insulin levels in humans were measured by a new assay, the isotope dilution assay (IDA), based on stable isotope dilution ***mass*** ***spectrometry***. A known amount of a deuterated analog of insulin was used as an ***internal*** ***standard*** and added to the serum samples before sample processing. After isolation by ***immunoaffinity*** chromatography and solid phase extraction, followed by a ***purification*** step on reversed-phase microbore high-performance liquid chromatography (HPLC), the insulin-containing fraction was analyzed by ***mass*** ***spectrometry***. The relative intensity of the signals due to insulin and its deuterated analog in the mass spectrum was used to determine the concentration of insulin in the sample. Using serum samples of 0.5-2.0 ml, we were able to measure insulin levels in the range of 3-1700 pmol/l in several clinical samples from type II diabetic patients. The basal level of endogenous insulin was also determined in two normal subjects and found to be approximately 20 pmol/l. Insulin secretion was followed after the ingestion of 75 g glucose in one healthy volunteer. Finally, the determination of the insulin level of one hemolyzed post-mortem blood sample, for which ***immunoassays*** gave inconsistent results, was performed to help forensic investigations. Our results showed a good correlation with standard ***immunoassay*** data, except in six samples where much lower values were obtained by our stable isotope dilution assay, suggesting an overestimation of insulin levels by ***immunoassay*** in some cases. As it is not subject to ***immunological*** interferences by insulin-related compounds, this new assay has a major clinical advantage in that it avoids confusions related to hyperinsulinemia.

L8 ANSWER 26 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1996:278304 BIOSIS

DOCUMENT NUMBER: PREV199699000660

TITLE: Quality control in the determination of cortisol in plasma/serum by using, on every sample, two different three-step separation methods including ultrafiltration, restricted-access high-performance liquid chromatography and reversed-phase high-performance liquid chromatography, and contrasting results to ***immunoassays***.

AUTHOR(S): Mueller, Hans W. (1); Eitel, Juergen

CORPORATE SOURCE: (1) Clinical Neurochemistry, Dep. Neurosurgery, Justus-Liebig-Univ., 35392 Giessen Germany

SOURCE: Journal of Chromatography B Biomedical Applications, (1996) Vol. 678, No. 2, pp. 137-150.
 ISSN: 0378-4347.

DOCUMENT TYPE: Article

LANGUAGE: English

AB Tests of HPLC columns with restricted access, polymer covered alumina, polymer, and different ODS phases showed that base-acid compatible ODS columns gave the best peak shapes of cortisol, ***internal*** ***standard***, as well as of plasma/serum (P/S) matrix components. Further trials with cortisol in P/S showed that three separation steps were essential in order to obtain chromatographic data which were superior to ***immunoassay*** data. Also, sufficient confidence in results required determination of each sample with two newly developed separation methods: (a) pre-separation with a restricted access column, concentration of the desired cut with a 20 mm base-acid compatible ODS column, and analysis with a 250 mm column filled with the same ODS; (b) pre-separation with an ultrafilter followed by the last two steps in (a). For detection UV was preferred over fluorescence. This twin multistep chromatography showed that ***immunoassays*** were very treacherous in that they produced a spectrum of results, ranging from good to untenable without any warning whatever about functionality. The measurement of official

controls, with reference values derived via gas chromatography-isotope dilution ***mass*** ***spectrometry***, also demonstrated the superiority of the double HPLC method.

L8 ANSWER 27 OF 43 MEDLINE DUPLICATE 5
 ACCESSION NUMBER: 96430191 MEDLINE
 DOCUMENT NUMBER: 96430191 PubMed ID: 8833319
 TITLE: Analysis of dexamethasone and betamethasone in bovine urine
 by ***purification*** with an "on-line"
 immunoaffinity chromatography-high-performance
 liquid chromatography system and determination by gas
 chromatography- ***mass*** ***spectrometry***.
 AUTHOR: Bagnati R; Ramazza V; Zucchi M; Simonella A; Leone F;
 Bellini A; Fanelli R
 CORPORATE SOURCE: Istituto di Ricerche Farmacologiche "Mario Negri," Milan,
 Italy.
 SOURCE: ANALYTICAL BIOCHEMISTRY, (1996 Mar 15) 235 (2) 119-26.
 Journal code: 0370535. ISSN: 0003-2697.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199705
 ENTRY DATE: Entered STN: 19970612
 Last Updated on STN: 19970612
 Entered Medline: 19970530

AB A method for the ***immunoaffinity*** extraction of dexamethasone and betamethasone in bovine urine, followed by high-pressure liquid chromatography (HPLC) fractionation and gas chromatography- ***mass*** ***spectrometry*** determination, is described. A commercial ***immunoaffinity*** gel, containing antibodies raised against dexamethasone, was used to prepare an ***immunoaffinity*** cartridge which was inserted in an automatic HPLC system for on-line extraction and ***purification***. By injecting urine samples (spiked with flumethasone as ***internal*** ***standard***) directly into the system, it was possible to collect ***purified*** fractions, containing the analytes of interest. The fractions were dried and derivatized to yield the tetra-trimethylsilyl derivatives of the three corticosteroids, which were analyzed by selected ion monitoring gas chromatography- ***mass*** ***spectrometry***. The method allowed a very good ***purification*** of samples and reached a detection limit of 0.1 ng/ml for dexamethasone and 0.2 ng/ml for betamethasone. Several samples, coming from a steer treated with dexamethasone and from other bovines coming from breedings in northern Italy, were analyzed with the method described. Dexamethasone levels ranged from 0.12 to 146 ng/ml.

L8 ANSWER 28 OF 43 MEDLINE DUPLICATE 6
 ACCESSION NUMBER: 95038653 MEDLINE
 DOCUMENT NUMBER: 95038653 PubMed ID: 7951151
 TITLE: ***Immunoaffinity*** extraction of 4-hydroxy-2-(4-methylphenyl)benzothiazole and its metabolites for determination by gas chromatography- ***mass*** ***spectrometry***.
 AUTHOR: Awata N; Toba F; Ando M; Shimada H; Miyairi S; Kato T; Goto J; Nambara T
 CORPORATE SOURCE: Product Research and Development Laboratories, Pharmaceuticals Research Center, Kanebo Ltd., Osaka, Japan.
 SOURCE: BIOLOGICAL AND PHARMACEUTICAL BULLETIN, (1994 Jun) 17 (6) 843-5.
 Journal code: 9311984. ISSN: 0918-6158.
 PUB. COUNTRY: Japan
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199412
 ENTRY DATE: Entered STN: 19950110
 Last Updated on STN: 19960129

Entered Medline: 19941212

AB ***Immunoaffinity*** extraction of 4-hydroxy-2-(4-methylphenyl)benzothiazole and its metabolites, together with the corresponding meta-isomers has been achieved by the use of an antibody raised against an ***immunogen***, an O-carboxymethylloxime-bovine serum albumin conjugate of 4-hydroxy-2-(4-formylphenyl)benzothiazole. The antibody produced exhibited a broad spectrum of affinity, not only for metabolites oxidized at the 4-methyl group of the benzene moiety but also for the corresponding meta-isomers. Up to 4 micrograms in total of these benzothiazoles could be extracted on the ***immunoaffinity*** adsorbent and recovered almost quantitatively by elution with 90% methanol. The resulting chromatogram was free from any interference. The eluted compounds were derivatized by conversion to their methyl esters and/or trimethylsilyl ethers, and subsequently separated into individual benzothiazoles by means of gas chromatography- ***mass*** ***spectrometry***. The derivatized compounds were monitored using a characteristic ion, $[M-CH_3]^+$, and the limit of detection was 10 fmole. The peak height ratio of each metabolite to its corresponding meta-isomer ***internal*** ***standard*** was plotted against the concentration of the former and good linearity was observed over the range 0.2-5 ng/ml.

L8 ANSWER 29 OF 43 MEDLINE DUPLICATE 7

ACCESSION NUMBER: 95021381 MEDLINE

DOCUMENT NUMBER: 95021381 PubMed ID: 7523910

TITLE: Detection of human exposure to carcinogens by measurement of alkyl-DNA adducts using ***immunoaffinity*** clean-up in combination with gas chromatography- ***mass*** ***spectrometry*** and other methods of quantitation.

AUTHOR: Shuker D E; Bartsch H

CORPORATE SOURCE: Unit of Environmental Carcinogens and Host Factors, International Agency for Research on Cancer, Lyon, France.

CONTRACT NUMBER: NCI CA48473 (NCI)

SOURCE: MUTATION RESEARCH, (1994 Oct-Dec) 313 (2-3) 263-8. Ref: 20
Journal code: 0400763. ISSN: 0027-5107.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199411

ENTRY DATE: Entered STN: 19941222

Last Updated on STN: 19960129

Entered Medline: 19941101

AB A brief overview is given of recent developments from our laboratory in the use of ***immunoaffinity*** clean-up in the determination of alkyl-DNA adducts. Compound- and group-specific antibodies have been prepared against 7-alkylguanines and 3-alkyladenines. The antibodies were attached to solid supports to make ***immunoaffinity*** columns which could then be used to selectively ***purify*** either single adducts or groups of adducts prior to quantitation by various methods. In the case of methyl adducts quantitation was achieved by ELISA (3-methyl-adenine, using a monoclonal antibody) and HPLC-electrochemical detection (7-methylguanine). For groups of adducts, quantitation of the individual compounds was effected by gas chromatography- ***mass*** ***spectrometry*** (3-alkyladenines, using deuterated analogues of each adduct as an ***internal*** ***standard***) and HPLC-fluorescence detection (7-alkylguanines). In all of these cases efficient ***purification*** of adducts from urine or DNA hydrolysates could be easily carried out. Using these techniques human exposure to alkylating agents in tobacco smoke and from cancer chemotherapy has been studied.

L8 ANSWER 30 OF 43 MEDLINE DUPLICATE 8

ACCESSION NUMBER: 94057450 MEDLINE

DOCUMENT NUMBER: 94057450 PubMed ID: 8238946

TITLE: ***Purification*** and analysis of drug residues in

urine samples by on-line ***immunoaffinity***
 chromatography/high-performance liquid
 chromatography/continuous-flow fast atom bombardment
 mass ***spectrometry*** .

AUTHOR: Davoli E; Fanelli R; Bagnati R
 CORPORATE SOURCE: Istituto di Ricerche Farmacologiche Mario Negri, Milano,
 Italy.
 SOURCE: ANALYTICAL CHEMISTRY, (1993 Oct 1) 65 (19) 2679-85.
 Journal code: 0370536. ISSN: 0003-2700.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199312
 ENTRY DATE: Entered STN: 19940117
 Last Updated on STN: 19980206
 Entered Medline: 19931213

AB An automatic system for the on-line extraction and analysis of
 diethylstilbestrol in the urine of rats and calves is described.
 Extraction was done by injecting samples directly into an
 immunoaffinity column containing antidiethylstilbestrol antibodies
 bound to a Sepharose matrix, and analysis was done by on-line
 high-performance liquid chromatography with ultraviolet and
 continuous-flow fast atom bombardment ***mass*** ***spectrometry***
 detectors. The system, consisting of one injector, two switching valves,
 and three pumps, was operated under computer control and allowed to
 perform a complete analysis of a sample in 28 min. An accurate
 quantitation by isotope dilution was also possible, by the use of
 deuterated diethylstilbestrol as ***internal*** ***standard*** .
 The sensitivity of the method, using selected-ion monitoring of the
 molecular ion of diethylstilbestrol, was 2 ng/mL, injecting 1 mL of urine
 sample. Results obtained from analyzing the urine of rats and calves
 treated with diethylstilbestrol are presented.

L8 ANSWER 31 OF 43 MEDLINE DUPLICATE 9
 ACCESSION NUMBER: 93008952 MEDLINE
 DOCUMENT NUMBER: 93008952 PubMed ID: 1382896
 TITLE: Specific and sensitive measurement of FK506 and its
 metabolites in blood and urine of liver-graft recipients.
 AUTHOR: Christians U; Braun F; Schmidt M; Kosian N; Schiebel H M;
 Ernst L; Winkler M; Kruse C; Linck A; Sewing K F
 CORPORATE SOURCE: Institute fur Allgemeine Pharmakologie, Medizinische
 Hochschule Hannover, FRG.
 SOURCE: CLINICAL CHEMISTRY, (1992 Oct) 38 (10) 2025-32.
 Journal code: 9421549. ISSN: 0009-9147.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199211
 ENTRY DATE: Entered STN: 19930122
 Last Updated on STN: 19960129
 Entered Medline: 19921116

AB A specific and sensitive assay for quantifying the
 immunosuppressant FK506 and its metabolites in blood and urine was
 developed. 32-O-Acetyl FK506 was synthesized and used as ***internal***
 standard . FK506 and its metabolites were ***purified*** from
 the samples by solid-liquid extraction and were injected into a
 high-performance liquid chromatographic (HPLC) system linked to a
 mass ***spectrometer*** (MS) by particle-beam interface. The
 FK506 derivatives were separated from interfering material by use of a 100
 x 4 mm C8 analytical column and water/acetonitrile or water/methanol
 gradient elution; they were detected by negative chemical ionization with
 methane as reagent gas. The limit of detection was 25 pg in a standard
 solution, and the limit of quantification in blood was 250 pg (extracted
 from 1 mL of blood). The CV was 11.3% at 5 ng, and no interferences with
 other drugs were found.

L8 ANSWER 32 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1991:483133 BIOSIS

DOCUMENT NUMBER: BA92:116893

TITLE: EVIDENCE OF ZEIN-BOUND IAA USING GAS CHROMATOGRAPHY-
SELECTED ION MONITORING- ***MASS*** ***SPECTROMETRY***
ANALYSIS AND ***IMMUNOGOLD*** LABELING.

AUTHOR(S): LEVERONE L A; KOSSENJANS W; JAYASIMIHULU K; CARUSO J L

CORPORATE SOURCE: DEP. BIOL. SCI., UNIVERSITY CINCINNATI, CINCINNATI, OHIO
45221.

SOURCE: PLANT PHYSIOL (BETHESDA), (1991) 96 (4), 1070-1075.

CODEN: PLPHAY. ISSN: 0032-0889.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Commercial zein was base-hydrolyzed and ***purified*** extracts were
subjected to gas chromatography-selected ion monitoring- ***mass***
spectrometry analysis. Indoleacetic acid (IAA) was shown to be
released from this storage protein of corn (Zea mays). Isotope dilution
using [¹³C₆]IAA as an ***internal*** ***standard*** revealed a
conservative ratio of 1 mole IAA to 175 moles zein. ***Immunoelectron***
micrographs of isolated protein bodies also showed IAA or an IAA-like
molecule associated with zein and deposited within these organelles.

L8 ANSWER 33 OF 43 MEDLINE DUPLICATE 10

ACCESSION NUMBER: 91225167 MEDLINE

DOCUMENT NUMBER: 91225167 PubMed ID: 2026720

TITLE: Analysis of methionine enkephalin in human pituitary by
multi-dimensional reversed-phase high-performance liquid
chromatography, radioreceptor assay, radioimmunoassay, fast
atom bombardment ***mass*** ***spectrometry***, and
mass ***spectrometry*** - ***mass***
spectrometry.

AUTHOR: Lovelace J L; Kusmierz J J; Desiderio D M

CORPORATE SOURCE: Department of Biochemistry, University of Tennessee,
Memphis 38163.

CONTRACT NUMBER: GM26666 (NIGMS)

SOURCE: JOURNAL OF CHROMATOGRAPHY, (1991 Jan 2) 562 (1-2) 573-84.

Journal code: 0427043. ISSN: 0021-9673.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199106

ENTRY DATE: Entered STN: 19910630

Last Updated on STN: 19910630

Entered Medline: 19910610

AB Methionine enkephalin (ME = YGGFM) was measured in five individual human
post-mortem pituitaries using four different analytical methods, with the
objective of comparing the molecular specificities of the methods.
Radioreceptor assay (RRA) used a receptor-rich preparation from brain and
[³H]etorphine as radioligand to determine ME-like receptoractivity
(ME-LR). Radioimmunoassay (RIA) measured ME-like ***immunoreactivity***
(ME-LI). Pituitary samples analyzed by RRA and RIA were ***purified***
first with a high-performance liquid chromatography (HPLC) gradient on a
polymer analytical column. Fast atom bombardment ***mass***
spectrometry (FAB-MS) in two different detection modes quantified
ME using the protonated molecular ion MH⁺ of ME at 574 a.m.u. and B/E
linked-field selected reaction monitoring (SRM) to monitor the specific
unimolecular metastable transition that produced the unique amino acid
sequence-determining tetrapeptide fragment ion YGGFA⁺ from the MH⁺
precursor ion. Both FAB-MS methods used the deuterated ***internal***
standard YGG[²H₅-F]M. Samples analyzed with FAB-MS were
purified first with multi-dimensional reversed-phase HPLC. The
first dimension was an ODS gradient, and the second dimension was a
polymer isocratic elution. The following ME amounts were measured (mean
+/- standard error of the mean): ME-LR, 7.0 +/- 1.9 micrograms g⁻¹ tissue;
ME-LI, 1.8 +/- 0.7 micrograms g⁻¹ tissue; MH⁺, 2.7 +/- 0.6 micrograms g⁻¹

tissue; SRM, 3.0 +/- 0.8 micrograms g-1 tissue. The FAB SRM method provided the highest level of molecular specificity amount these four analytical methods used to measure picomole amounts of endogenous ME in a human pituitary.

L8 ANSWER 34 OF 43 MEDLINE DUPLICATE 11
 ACCESSION NUMBER: 92003154 MEDLINE
 DOCUMENT NUMBER: 92003154 PubMed ID: 1912292
 TITLE: Isolation of urinary 3-methyladenine using
 immunoaffinity columns prior to determination by
 low-resolution gas chromatography- ***mass***
 spectrometry
 AUTHOR: Friesen M D; Garren L; Prevost V; Shuker D E
 CORPORATE SOURCE: International Agency for Research on Cancer, Lyon, France.
 CONTRACT NUMBER: CA48473 (NCI)
 SOURCE: CHEMICAL RESEARCH IN TOXICOLOGY, (1991 Jan-Feb) 4 (1)
 102-6.
 Journal code: 8807448. ISSN: 0893-228X.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199111
 ENTRY DATE: Entered STN: 19920124
 Last Updated on STN: 19920124
 Entered Medline: 19911104

AB An ammonium sulfate precipitated ***immunoglobulin*** G (IgG) fraction from rabbit antiserum, prepared by use of novel haptenic derivatives, was used to make ***immunoaffinity*** columns for ***purification*** of 3-methyladenine (3-MeAde) from human urine. IgG was covalently bound to protein A-Sepharose, and the resulting affinity gel columns were sufficiently stable for multiple reuse. 3-MeAde (up to 200 ng) was adsorbed at pH 7.4 and, after extensive washing, eluted with 1 M acetic acid. Recovery of 3-MeAde was typically greater than 90%. For gas chromatography- ***mass*** ***spectrometry*** analysis, deuterium-labeled (d3) 3-MeAde (50 ng per sample) was used as an ***internal*** ***standard***. 3-MeAde was determined as the mono-tert-butylidimethylsilyl derivative and quantitated by measurement of ions at m/z 206 (3-MeAde-d0) and m/z 209 (3-MeAde-d3). Repeated analyses of a human urine sample show excellent reproducibility of the method.

L8 ANSWER 35 OF 43 MEDLINE
 ACCESSION NUMBER: 91004055 MEDLINE
 DOCUMENT NUMBER: 91004055 PubMed ID: 2208155
 TITLE: Determination of O6-butylguanine in DNA by
 immunoaffinity extraction/gas chromatography-
 mass ***spectrometry***
 AUTHOR: Bonfanti M; Magagnotti C; Galli A; Bagnati R; Moret M;
 Gariboldi P; Fanelli R; Airoidi L
 CORPORATE SOURCE: Laboratorio di Farmacologia e Tossicologia Ambientali,
 Istituto di Ricerche Farmacologiche, Mario Negri, Milan,
 Italy.
 SOURCE: CANCER RESEARCH, (1990 Nov 1) 50 (21) 6870-5.
 Journal code: 2984705R. ISSN: 0008-5472.
 PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 199011
 ENTRY DATE: Entered STN: 19910117
 Last Updated on STN: 19910117
 Entered Medline: 19901121

AB A sensitive, specific, and rapid method for quantitating the minor adduct O6-butylguanine (O6BuG) in hydrolyzed DNA has been developed by combining ***immunoaffinity*** chromatography and high resolution gas chromatography-negative ion chemical ionization- ***mass*** ***spectrometry***. Polyclonal antibodies raised against O6BuG were

coupled to CNBr-activated Sepharose 4B and used for sample clean-up and extraction of the specific O6-alkylguanine. After addition of O6BuG and its deuterium labeled analogue (O6BuG-D7), used as ***internal***
 standard, hydrolyzed DNA was applied on the ***immunoaffinity*** column and washed with water, and the ***immunoabsorbed*** butylated guanines were eluted with acetone/water (95/5) before gas chromatographic derivatization. O6BuG and O6BuG-D7 were analyzed and quantitated by high resolution gas chromatography-negative ion chemical ionization- ***mass*** ***spectrometry*** as their pentafluorobenzyl-trimethylsilyl derivatives. ***Immunoaffinity*** column capacity and O6BuG recovery from this column were 1.53 nmol O6BuG/column and 62 +/- 5%, respectively. The method was applied to evaluate O6BuG levels in DNA butylated in vitro with 10 mM N-nitroso-N-butylurea or isolated from rats given an i.p. dose of 185 mg/kg N-nitroso-N-butylurea or N-nitrosodibutylamine. In the first case the level of modifications present in calf thymus DNA was 104 mumol O6BuG/mol guanine, and in the second case O6BuG in liver DNA was about 6 times higher after N-nitroso-N-butylurea (2.11 mumol O6BuG/mol guanine) than after N-nitrosodibutylamine (0.34 mumol O6BuG/mol guanine) treatment. These results indicate that O6BuG formed in vivo can be isolated and quantitated by this method, which may also be useful for studying DNA damage and repair mechanisms.

L8 ANSWER 36 OF 43 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 1990:172395 CAPLUS

DOCUMENT NUMBER: 112:172395

TITLE: Feasibility of using [18O2]11-dehydrothromboxane B2 as an ***internal*** ***standard*** of ***immunoaffinity*** ***purification*** followed by gas chromatography/selected ion monitoring

AUTHOR(S): Ishibashi, Masataka; Ohyama, Yoshiharu; Watanabe, Keiko; Hayashi, Yoko; Takasaki, Wataru; Nakagawa, Akihiko; Mizugaki, Michinao

CORPORATE SOURCE: Pharm. Group, Nippon Kayaku Co., Ltd., Tokyo, 115, Japan

SOURCE: Chem. Pharm. Bull. (1989), 37(11), 3171-3

CODEN: CPBTAL; ISSN: 0009-2363

DOCUMENT TYPE: Journal

LANGUAGE: English

AB [1,1-18O2]11-dehydrothromboxane B2 (11-dehydro-TXB2) was prepd. by repetitive base-catalyzed hydrolysis of the lactone ring of its [1,1,11-18O3]-analog, and evaluated for its suitability as an internal std. in gas chromatog./selected ion monitoring (GC/SIM) of 11-dehydro-TXB2. Use of the present [18O2]-analog as an internal std. may make it a suitable candidate for specific ***immunoaffinity*** ***purifn*** followed by GC/SIM.

L8 ANSWER 37 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE
12

ACCESSION NUMBER: 1987:467061 BIOSIS

DOCUMENT NUMBER: BA84:112501

TITLE: COMPARISON OF A COMMERCIAL ELISA ASSAY FOR IAA AT SEVERAL STAGES OF ***PURIFICATION*** AND ANALYSIS BY GAS CHROMATOGRAPHY-SELECTED ION MONITORING- ***MASS*** ***SPECTROMETRY*** USING A 6 CARBON-13-LABELED ***INTERNAL*** ***STANDARD***

AUTHOR(S): COHEN J D; BAUSHER M G; BIALEK K; BUTA J G; GOCAL G F W; JANZEN L M; PHARIS R P; REED A N; SLOVIN J P

CORPORATE SOURCE: U.S. DEP. AGRIC., AGRIC. RES. SERV., PLANT HORMONE LAB., BELTSVILLE AGRIC. RES. CENT.-W., BELTSVILLE, MD. 20705.

SOURCE: PLANT PHYSIOL (BETHESDA), (1987) 84 (4), 982-986.

CODEN: PLPHAY. ISSN: 0032-0889.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB Quantitative analysis of indole-3-acetic acid (IAA) using selected ion monitoring gas chromatography- ***mass*** ***spectrometry*** (GC-MS) with 13C6]benzene ring]-IAA as the ***internal***

standard was used to compare the quantitative accuracy of commercial enzyme-linked ***immunoabsorbent*** assay (ELISA) kits. Plant materials differed in the amount of ***purification*** required prior to use of ELISA for reliable estimates to be made.

Purification similar to that obtained by at least one high performance liquid chromatographic (HPLC) step was generally necessary prior to ELISA analysis of plant materials. Additional levels of ***purification*** appeared to be required for some plant materials prior to HPLC in order to obtain an accurate estimate by ELISA techniques. In no case was it possible to obtain reasonable estimates of IAA from crude extracts or even from acidic fractions of extracts of plant tissues. GC-MS techniques provide a rapid and simple method for checking the validity of ELISA techniques. Quantitative GC-MS, or a similar technique that provides an independent quantitative validation, should, whenever possible, be applied to each new plant material under study if use of the ELISA is planned.

L8 ANSWER 38 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1988:32607 BIOSIS

DOCUMENT NUMBER: BA85:20332

TITLE: THE DEVELOPMENT OF AN INDIRECT ELISA FOR ABSCISIC ACID.

AUTHOR(S): ROSS G S; ELDER P A; MCWHA J A; PEARCE D; PHARIS R P

CORPORATE SOURCE: DEP. AGRIC. BOTANY, QUEEN'S UNIV. BELFAST, BELFAST BT9 5PX, NORTHERN IRELAND.

SOURCE: PLANT PHYSIOL (BETHESDA), (1987) 85 (1), 46-50.

CODEN: PLPHAY. ISSN: 0032-0889.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB An indirect method of enzyme-linked- ***immunosorbent*** -assay (ELISA)

is reported for abscisic acid (ABA), utilising a thyroglobulin-ABA conjugate for coating wells. The assay can use commercially available monoclonal antibodies, is sensitive to as little as 20 picograms ABA per well, and is much more conservative of antibody than direct methods. The most dilute ABA standards did not retain their antigenicity during storage, so ABA standard sets were diluted immediately prior to use. The indirect ELISA was used successfully to estimate ABA concentrations in developing cotyledons of *Pisum sativum* L., after only little preliminary ***purification***. It was validated for this tissue through the use of gas chromatography-electron capture detection (GC-EC), and capillary GC-selected ion monitoring (GC-MS-SIM) using [2H4]ABA as an ***internal*** ***standard***. Full spectrum GC- ***mass*** ***spectrometry*** was also used to verify that ABA was present in a sample assayed quantitatively by both ELISA and GC-MS-SIM.

L8 ANSWER 39 OF 43 MEDLINE

ACCESSION NUMBER: 83156158 MEDLINE

DOCUMENT NUMBER: 83156158 PubMed ID: 6831697

TITLE: ***Immunoabsorption*** to improve gas chromatography/high-resolution ***mass*** ***spectrometry*** of estradiol-17 beta in plasma.

AUTHOR: Gaskell S J; Brownsey B G

SOURCE: CLINICAL CHEMISTRY, (1983 Apr) 29 (4) 677-80.

Journal code: 9421549. ISSN: 0009-9147.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198305

ENTRY DATE: Entered STN: 19900318

Last Updated on STN: 19900318

Entered Medline: 19830505

AB We describe a new, highly selective procedure for the determination of estradiol-17 beta in plasma. Samples are extracted with a micro-cellulose-coupled antiserum to estradiol-17 beta. Conversion of the extracted steroid to the bis(trimethylsilyl) ether is followed by gas chromatography/high-resolution ***mass*** ***spectrometry*** with selected ion monitoring. Precise quantification is achieved through the

use of [2H3]estradiol-17 beta as ***internal*** ***standard*** .

L8 ANSWER 40 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1983:319136 BIOSIS

DOCUMENT NUMBER: BA76:76628

TITLE: RADIO ***IMMUNOASSAY*** FOR DI ETHYL STILBESTROL AND
THE MONO GLUCURONIDE METABOLITE IN BOVINE LIVER.

AUTHOR(S): GRIDLEY J C; ALLEN E H; SHIMODA W

CORPORATE SOURCE: DIV. VET. MED. RES., FOOD DRUG ADM., BELTSVILLE, MD. 20705.

SOURCE: J AGRIC FOOD CHEM, (1983) 31 (2), 292-296.

CODEN: JAFCAU. ISSN: 0021-8561.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB The complex matrix in liver causes difficulties in development of a radioimmunoassay (RIA) to quantify compounds bound in liver. An RIA method was developed for diethylstilbestrol (DES) in bovine liver and employed a ***purification*** procedure to circumvent these problems; the procedure included liquid-liquid partitioning, Sephadex LH-20 chromatography and quantitative enzymatic hydrolysis of the principal metabolite, DES glucuronide. Assay background due to liver matrix was 0.05 ppb (1/109). Average recovery of DES and its monoglucuronide from fortified liver was 43% by RIA. 3H-DES used as an ***internal*** ***standard*** had a higher apparent recovery (67.7%) by liquid scintillation counting. With an in vivo contaminated liver, accuracy was confirmed by a gas chromatography- ***mass*** ***spectrometry*** method. By repeating the extraction and RIA without enzymatic hydrolysis on this same liver, the free DES was calculated to be 7.8%. The limit of determination for this method with 95% confidence limits was 0.3 ppb.

L8 ANSWER 41 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1983:229818 BIOSIS

DOCUMENT NUMBER: BA75:79818

TITLE: IDENTIFICATION OF THYROXINE IN HUMAN BREAST MILK BY GAS
CHROMATOGRAPHY ***MASS*** ***SPECTROMETRY***

AUTHOR(S): MOLLER B; BJORKHEM I; FALK O; LANTTO O; LARSSON A

CORPORATE SOURCE: DEP. CLIN. CHEM., HUDDINGE UNIV. HOSP., S-141 86 HUDDINGE, SWED.

SOURCE: J CLIN ENDOCRINOL METAB, (1983) 56 (1), 30-34.

CODEN: JCEMAZ. ISSN: 0021-972X.

FILE SEGMENT: BA; OLD

LANGUAGE: English

AB In several previous publications it was reported that human breast milk contains significant amounts of T4 [thyroxine]. Great differences in concentrations were found by different authors. In all of these publications T4 was assayed by RIA [radioimmunoassay], and it seems probable that the varying results obtained are due to varying specificity of the antibodies used in the assay. Definite demonstration of the presence of T4 in breast milk requires a more specific method than RIA. In the present work combined gas chromatography- ***mass*** ***spectrometry*** was used. T4 was isolated from human breast milk by combined anion- and cation-exchange chromatography. The ***purified*** material was treated with HCl in methanol and trifluoroacetic acid anhydride and was analyzed by single-ion monitoring of the ions at m/e 983, m/e 870, and m/e 799, major ions in the mass spectrum of the N,O-bis(trifluoroacetyl) methyl ester of T4. Significant peaks confirmed the presence of T4 in human milk. The estimated concentration was less than 10 ng/ml. Attempts were made to quantitate the T4 by selected ion monitoring of the ions at m/e 870 and m/e 822 after addition of monobromotriiodothyronine as ***internal*** ***standard*** . According to this latter method, the concentration of T4 in 4 samples of centrifugated breast milk was less than 4 ng/ml. The possible physiological significance of the finding is discussed.

L8 ANSWER 42 OF 43 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

ACCESSION NUMBER: 1982:145712 BIOSIS

DOCUMENT NUMBER: BA73:5696

TITLE: VALIDATION OF A RADIO ***IMMUNOASSAY*** FOR IAA USING

GAS CHROMATOGRAPHY SELECTED ION MONITORING ***MASS***
SPECTROMETRY

AUTHOR(S): PENGELLY W L; BANDURSKI R S; SCHULZE A
 CORPORATE SOURCE: DEPARTMENT OF BOTANY AND PLANT PATHOLOGY, MICHIGAN STATE
 UNIVERSITY, EAST LANSING, MICHIGAN 48824.
 SOURCE: PLANT PHYSIOL (BETHESDA), (1981) 68 (1), 96-98.
 CODEN: PLPHAY. ISSN: 0032-0889.
 FILE SEGMENT: BA; OLD
 LANGUAGE: English

AB A radioimmunoassay for IAA was validated by comparison with a physico-chemical assay utilizing gas chromatography-selected ion monitoring- ***mass*** ***spectrometry*** and 4,5,6,7-tetradeutero-IAA as an ***internal*** ***standard***. The radioimmunoassay provided a reliable estimate of the free IAA content of etiolated corn [Zea mays cv. Stowell's Evergreen Sweet Corn] shoots. Base hydrolysis of extracts for determination of ester IAA released substances which interfered with the radioimmunoassay. Interference was detected by internal controls and by lack of agreement with the mass spectral method. Interfering compounds could be removed from extracts by chromatography on diethylaminoethyl- and hydroxypropylated (lipophilic) Sephadex G-25. Following such ***purification*** the radioimmunoassay estimate of the total (free + ester) IAA content of etiolated corn shoots agreed with the mass spectral method within 2% on the average.

L8 ANSWER 43 OF 43 EMBASE COPYRIGHT 2002 ELSEVIER SCI. B.V.

ACCESSION NUMBER: 81000162 EMBASE

DOCUMENT NUMBER: 1981000162

TITLE: Determination of phenol in injectable biological products
by gas chromatography.

AUTHOR: May J.C.; Del Grosso A.V.; Barron R.P.

CORPORATE SOURCE: DHEW, PHS, Food Drug Adm. Bur. Biol., Bethesda, Md. 20205,
United States

SOURCE: Journal of Biological Standardization, (1980) 8/3
(209-218).

CODEN: JBSTBI

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal

FILE SEGMENT: 004 Microbiology

037 Drug Literature Index

LANGUAGE: English

AB A gas chromatographic method for the determination of phenol in a wide variety of biological products has been developed by extending a USP procedure. The procedure and its extension were validated for preparations of cholera vaccine, typhoid vaccine, tuberculin ***purified*** protein derivative, pneumococcal polysaccharide vaccine, horse serum-derived products such as antivenins, several types of aqueous, glycerinated and alum precipitated allergenic extracts and others. The average recovery of phenol at the 0.3-0.5% phenol level was 99.6%. The average precision was measured as a relative standard deviation of 0.43%. Glycerin contained in glycerinated allergenic extracts and tuberculin ***purified*** protein derivative did not interfere with quantitation. Horse serum-derived antitoxins, antivenins and antirabies serum produced a precipitate upon the addition of the ***internal*** ***standard*** solution, benzyl alcohol in 100% methanol. This precipitate was eliminated by the use of 5% (or 0%) methanol in water as diluent in the ***internal*** ***standard*** solution. Two aqueous allergenic extracts were encountered that produced peaks that were not adequately resolved from the phenol and benzyl alcohol peaks. Lowering the injection temperature to 185.degree.C and the column temperature to 125.degree.C produced satisfactory separations. Gas chromatography/ ***mass*** ***spectrometry*** was used to determine the purity of peaks representing benzyl alcohol and phenol in tuberculin, cholera vaccine, typhoid vaccine and several allergenic extracts.

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(FILE 'HOME' ENTERED AT 13:24:36 ON 10 OCT 2002)

FILE 'MEDLINE, EMBASE, BIOSIS, CAPLUS' ENTERED AT 13:25:35 ON 10 OCT 2002

L1 13823 S MASS SPECTROMETRY AND IMMUNO?
L2 30373 S INTERNAL STANDARD
L3 278 S L1 AND L2
L4 153 DUP REM L3 (125 DUPLICATES REMOVED)
L5 362566 S IMMUNO? AND PURIF?
L6 373829 S MASS SPECTROMET? OR MALDI OR (TIME OF FLIGHT)
L7 61 S L5 AND L6 AND L2
L8 43 DUP REM L7 (18 DUPLICATES REMOVED)